concld. 46-47

acetamido-7-aza-2-indolinone, 3-(2-ethyl-3-methylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-isopropyl-3-methylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-cyclohexyl-3-methylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-phenylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(3-methyl-2-n-propylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-n-butylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-benzyl-4-methylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-n-propylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(4-acetyl-2-ethoxycarbonyl-3-methylpyrrol-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(4-methoxycarbonyl-3-methoxycarbonylmethyl-2-methylpyrrol-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-[4-(4-chlorobenzoyl)-1-methylpyrrol-2-methylidenyl]-5-acetamido-7-aza-2-indolinone, 3-[2-[1-methyl-5-(trifluoromethyl)pyrrol-3-yl]thien-5-methylidenyl]-5-acetamido-7-aza-2-indolinone, 3-[2-[1-methyl-3-(trifluoromethyl)pyrrol-5-yl]thien-5-methylidenyl]-5-acetamido-7-aza-2-indolinone, 3-(3-phenoxythien-2-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(4-phenylethynylthien-2-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(2-phenylethynylthien-5-methylidenyl)-5-acetamido-7-aza-2-indolinone, 3-(3-methylbenzothien-2-methylidenyl)-5-acetamido-7-aza-2-indolinone, and 3-[2-(2-carboxyethyl)-3-methylpyrrol-2-methylidenyl]-5-acetamido-7-aza-2-indolinone.

Please add new claim 46 as follows:

C8

--46. A method for preventing a protein tyrosine kinase related disorder in an organism comprising administering a therapeutically effective amount of said pharmacological composition of claim 19 to said organism.--

REMARKS

The title of the application has been amended. The specification has also been amended to include language priority language that matches the examiner's suggestion.

More legible copies of pages 41-54 of the specification have also been provided. No new matter has been added.

Claims 1-9, 11-16, 18-37 and 41-45 are pending in the application. Claim 18 is allowed. Claims 1-9, 11-16, 19-37 and 41-45 are rejected. Claims 1-9, 11-16, 19-21, 41 and 42 have been amended. Claim 46 has been added.

Information Disclosure Statement

Applicants have attached as Apendix I copies of the French patent (AJ), Hungarian patent (AK), Beilstein Reg. No. 252929 and a courtesy copy of U. S. Patent No. 5,721,237, also filed seperately with a Form 1449.

Specification

Applicants have also submitted as Appendix II a more legible copy of pages 41-54 to replace the current pages of the specification. In addition, applicants have used the examiner's suggestion to amend the statement regarding filing dates.

Rejections under 35 USC §112, First Paragraph

Claims 1-9, 11-16, 19 and 20 are rejected under 35 USC § 112, first paragraph, for lack of written description. Applicants traverse this rejection. The examiner has failed to demonstrate that the claimed invention lacks written description. In this regard, prodrugs are discussed on page 6. However, in the interest of expediting prosecution, applicants have deleted the term "prodrug" from the pending claims, rendering this rejection moot. Applicants maintain that this amendment was not made for purposes of patentability and do not intend to surrender any prodrug equivalents of the present invention.

Claims 21-37 have been rejected under 35 USC § 112, first paragraph, for lack of written description. Applicants traverse. Applicants maintain that the application provides ample support for "prevention" of various disorders. However, in the interest of expediting prosecution, applicants have deleted the term "prevention" from Claim 21, rendering this reject moot.

Rejections under 35 USC §112, Second Paragraph

Claims 1-9, 11-16, 19-37 and 41-45 were rejected under 35 USC § 112, second paragraph, for indefiniteness. Applicants traverse this rejection and request reconsideration for parts of the rejection based on the following remarks. In the alternative, applicants have made the following amendments to the claims, thereby rendering this rejection moot.

a) Claims 1 and 41 have been amended to define the terms C-carboxyl, O-carboxyl, C-amido, guanyl and sulfonyl, as defined in specification. Support for these amendments is found, *inter alia*, at pages 12 and 13 of the specification.

b) Applicants contend that one of ordinary skill in the art can understand the term "O-thiocarbamyl," as it is defined at page 13 of the specification. It is a "well-established axiom in patent law that a patentee is free to be his or her own lexicographer" See MPEP § 2173.05, citing *Hormone Research Foundation Inc. v. Genentech Inc.*, 904 F.2d 1558 (Fed. Cir. 1990). Moreover, "Definiteness of claim language must be analyzed, not in a vacuum, but in light of the content of the particular application disclosure." See MPEP § 2173.02.

c) The term "trimethane carbonyl" has been added to Claim 1, thus providing for antecedent basis in Claim 16.

d) Claim 20 has been amended as follows:

> "20. A method for the modulation of the catalytic activity of a protein tyrosine kinase comprising administering said **[compound, salt or prodrug]** <u>**compound or salt**</u> of claim 1 to said protein tyrosine kinase."

Applicants cannot respond to the rejection over the use of the phrase "comprising administering a therapeutically effective amount" as it does not appear in Claim 20.

e) Applicants have added the contents of Table 1 into Claims 42 and 43.

f) Applicants contend that the term "met related disorder" would be understood by one of ordinary skill in the art. In support of this, they have attached as Appendix III, four articles, including one review article, all predating the earliest filing date of the present application and describing the met receptor. The appended articles are as follows: Rosen et al., "Scatter Factor and Angiogenesis," <u>Advances in Cancer Research</u>, 67:257-267; 279 (1995); Kanda et al., "HGF-HFGR-*c-met* SYSTEM AND CARCINOGENESIS," <u>Gann</u>

Monograph on Cancer Research Vol 42, 153-161 (1994); Zarnegar et al., "The Many Faces of Hepatocyte Growth Factor: from Hepatopoiesis to Hematopoiesis," The Journal of Cell Biology, Vol 129, 1177-1180 (1995); and Matsumoto et al., "Emerging Multipotent Aspects of Hepatocyte Growth Factor," J.Biochem, Vol 119, 591-600 (1996).

In view of these amendments and remarks, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 USC § 103

Claims 1-5, 9, 11, 12, 16, 19-37 and 41-45 are rejected under 35 USC § 103 as being unpatentable over Buzzetti. Applicants respectfully traverse this rejection. The Examiner has failed to demonstrate that the invention is *prima facie* obvious, based on Buzetti. The Examiner provides no evidence that the art specifically suggests the claimed compounds. Moreover, the "A group" of Buzzetti is described as "benzene, napthalene, 5,6,7,8,-tetrahydronapthalene, quinoline, isoquinoline, indole or 7-azaindole," whereas the present claims recite 5-membered monocyclic rings, such as pyrrole, imidazole and thiophene. Thus, the compounds of the present claims are not suggested by Buzzetti, which only discloses bicyclic rings for the A group. Accordingly, applicants request reconsideration and withdrawal of this rejection.

CONCLUSION

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited.

The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

Respectfully submitted,

1/18/01
Date

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.